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Patent, Trademark and Copyright Causes, Unfair Competition, Trade Secrets, Licensing, Litigation

TO: **USPTO**
1-571-273-8300

Date: March 9, 2009
FROM: THE NATH LAW GROUP

RE: **Executed Rule 132 Declaration**
U.S. Serial Number 10/539,769
Inventor: Sauvaigo, S.
Filed: December 1, 2005
Our Ref. 40522U

NO. OF PAGES (including this page): 6

COMMENTS AND/OR SPECIAL INSTRUCTIONS:

Dear Commissioner:

Further to the Response/Request for Reconsideration of February 27, 2009, attached herewith is an executed Rule 132 Declaration.

An unexecuted version thereof was filed with the Response of February 27, 2009.

Accordingly, it is believed this application is now in condition for allowance.

Date: March 9, 2009

By: _____
William E. Beaumont
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PATENT

Attorney Docket No. 40522U

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Application of: Sauvaigo, S.

Serial No.: 10/539,769

Filed: December 1, 2005

Confirmation No.: 6482

Art Unit: 1636

Examiner: Joike, Michele K.

For: METHOD FOR THE QUANTITATIVE ASSESSMENT OF GLOBAL AND SPECIFIC DNA REPAIR CAPACITIES OF AT LEAST ONE BIOLOGICAL MEDIUM, AND THE APPLICATIONS THEREOF

DECLARATION UNDER RULE 132

Commissioner of
Patents PO Box 1450
Alexandria, VA 22313-1450

Dear Commissioner:

Now comes Sylvie Sauvaigo, who declares and states that:

1. I have the following degrees and qualifications including the ability to direct PhD theses: PhD in Biology, M.S. in Molecular Chemistry, and a B.S. in Biochemical Engineering.

2. I have been employed by COMMISSARIAT A L'ENERGIE ATOMIQUE (CEA) since October 15th, 1985.

3. I declare that I am experienced in the field of DNA modification, molecular biology and biology, as well as DNA damage and DNA repair mechanisms as may be seen from the attached truncated curriculum vitae and the publication list attached hereto.

4. I am the named inventor of the above-identified patent application ("the '769 Application").

5. I have reviewed the Office Action dated September 4, 2008, and note that the question of what does and does not constitute supercoiled DNA has been raised by the examiner.

6. The claimed method, and in particular claim 22, uses exclusively supercoiled DNA targets, which contain a random assortment of specific lesions which require DNA excision and resynthesis, and, hence, act as a reagent upon

which the DNA excision and resynthesis repair capacities can be both selectively and quantitatively measured.

7. A general methodology for this field is described in the reference book "Molecular Cloning: A Laboratory Manual" by J. Sambrook, E.F. Fritsch and T. Maniatis, Cold Spring Harbor N.Y., (1989). A publication which more precisely illustrates how supercoiled DNA can be characterized by its electrophoresis pattern on agarose gel is (Quantitation of supercoiled circular content in plasmid DNA in solutions using a fluorescence based method, in Nucleic Acids Research (2000), vol. 28, n° 12, e57).

8. Therefore, such a given circular plasmid will have a specific migration pattern on agarose gel in a given set of conditions. A supercoiled version of this same circular plasmid as in claim 22, will have a different migration pattern in agarose gel due to its supercoiled state.

9. The fact that the target DNA used in the method of claim 22 is supercoiled, is essential as this means that no DNA strand breaks and/or no nuclease digestion has occurred upon the target plasmid. This is because DNA strand breaks inherently lead to a relaxation of super coiled DNA into its base or normal helical structure, as a strand break allows the DNA molecule to attempt to modify its structure so as to remove additional twists.

10. This allows the method according to claim 22, to provide a quantitative assessment of the DNA excision and resynthesis repair mechanisms of the biological sample being tested, while excluding those repair mechanisms which act to repair strand breaks and/or nuclease digestion. Thus, the claimed method is selective for quantitatively assessing DNA excision and resynthesis repair mechanisms.

11. I have also noted that the examiner stated in the Office Action of September 4, 2008, that the DNA used in US 2002/0022228 ('228) is supercoiled, however this is not correct. In '228, experiments are conducted using short synthesized oligonucleotides ("oligos") of between 30-40 bp in length. Such short non-circular oligos inherently are not supercoiled according to the definition of the cited references and as understood by one having ordinary skill in the art. Thus, the topology of these short oligonucleotides cannot be distinguished using electrophoresis pattern migration in agarose gel as described for supercoiled plasmids.

12. Thus, I am of the opinion based on both the literature noted above and the knowledge of those of ordinary skill in the art that the '228 publication does not relate to

supercoiled DNA.

13. I am further of the opinion that one skilled in the art would not have been put in possession of the claimed invention by the '228 publication.

14. The above conclusions are also buttressed by the different methodologies between the claimed invention and the '228 publication. Notably, in the '228 publication short bound single or double stranded oligonucleotides of known sequence are provided which contain one or more defects such as a base mismatch or apurinic site mimicking a mutation which requires excision and resynthesis repair. Samples are then applied to the bound oligos and incorporated labeled nucleotides are used to determine the repair capacity of the tested sample. This methodology only measures DNA repair mechanisms which act upon the selected mutations or lesions which diminishes the recorded effects of the other repair mechanisms.

In contrast, in the claimed invention supercoiled plasmids are used to test the repair capacities of a biological sample or medium. These altered plasmids are purified so that only supercoiled plasmids are isolated, which means that plasmids which have undergone a strand break or which more generally have a relaxed structure are eliminated. The remaining supercoiled plasmids which contain a random assortment of other types of lesions requiring DNA excision and resynthesis can act as a reagent upon which DNA excision and repair capacities of the biological medium can be measured as noted above in a selective and quantitative manner.

15. I am also of the opinion that neither the '228 publication alone or in combination with any one or combination of You et al, Douki, Meselson et al, Chiu et al, Zierdt et al, Gelfrand et al, Yershor et al and/or Randerath et al would have rendered the claimed invention obvious to one skilled in the art at the time the claimed invention was made as none of these cited references, either alone or in combination, would have motivated one skilled in the art to use supercoiled DNA targets exclusively to quantitatively assess the excision and resynthesis capabilities of a biological sample.

16. Finally, I am of the opinion that the claimed invention presents advantages over the method of the '228 publication since although the exact lesions are unknown for the modified supercoiled plasmids, because the target plasmids contain a large number of modification types in a wide variety of locations, such a heterogeneous target reagent can more accurately quantify all of the various DNA excision and resynthesis repair capacities of a biological medium than can a target reagent consisting of a large number of single type

mutations/lesions as in '228.

17. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing there from.

Date: March 6th 2009

Sylvie Sauvaigo